A

Azulene

Guaiazulene

B

TS (D/B)

1: R= (CH$_2$)$_2$NH$_2$ — 1.9
2: R= (CH$_2$)$_3$NH$_2$ — 2.0
3: R= (CH$_2$)$_4$NH$_2$ — 1.1
4: R= (CH$_2$)$_5$NH$_2$ — 1.2
5: R= (CH$_2$)$_6$NH$_2$ — 1.1
6: R= (CH$_2$)$_3$O(CH$_2$)$_3$NH$_2$ — 1.1
7: R= (CH$_2$)$_3$N(CH$_3$)$_2$ — 1.4
8: R= (CH$_2$)$_2$O(CH$_2$)$_2$O(CH$_2$)$_2$NH$_2$ — 1.7
9: R= (CH$_2$)$_2$S(CH$_2$)$_2$NH$_2$ — 1.4
10: R= [ring] — 2.3

Uehara et al. （Ref. 13）

C

TS (D/B)

1: R=(CH$_2$)$_2$CH$_3$ — >28.9
2: R=(CH$_2$)$_3$CH$_3$ — ><1.7
3: R=(CH$_2$)$_4$CH$_3$ — >1.3
4: R=(CH$_2$)$_2$OH — 4.6
5: R=(CH$_2$)$_3$OH — 2.0
6: R=(CH$_2$)$_2$OCH$_3$ — 4.0
7: R=(CH$_2$)$_3$OCH$_3$ — 5.2
8: R=(CH$_2$)$_3$NH$_2$ — 1.2
9: R=(CH$_2$)$_4$NH$_2$ — 1.1
10: R=((CH$_2$)$_2$O)$_2$(CH$_2$)$_2$NH$_2$ — 1.4

Wada et al. （Ref. 14）

D

1–7

1 : R=(CH$_2$)$_2$CH$_3$ 1.1
2 : R=(CH$_2$)$_3$CH$_3$ 1.7
3 : R=(CH$_2$)$_4$CH$_3$ 3.9
4 : R=(CH$_2$)$_2$OH 1.0
5 : R=(CH$_2$)$_3$OH 0.8
6 : R=(CH$_2$)$_2$OMe 0.9
7 : R=(CH$_2$)$_3$OMe 1.1

8–14

8 : R=(CH$_2$)$_2$CH$_3$ 7.1
9 : R=(CH$_2$)$_3$CH$_3$ 3.7
10 : R=(CH$_2$)$_4$CH$_3$ 2.4
11 : R=(CH$_2$)$_2$OH 1.8
12 : R=(CH$_2$)$_3$OH 1.9
13 : R=(CH$_2$)$_2$OMe 1.8
14 : R=(CH$_2$)$_3$OMe 1.9

15–21

15 : R=(CH$_2$)$_2$CH$_3$ 2.3
16 : R=(CH$_2$)$_3$CH$_3$ 2.4
17 : R=(CH$_2$)$_4$CH$_3$ 2.3
18 : R=(CH$_2$)$_2$OH 1.0
19 : R=(CH$_2$)$_3$OH 1.0
20 : R=(CH$_2$)$_2$OMe 1.1
21 : R=(CH$_2$)$_3$OMe 1.2

Imanari et al. （Ref. 15）

E

R=

1: (CH$_2$)$_2$OH — 1.0
2: (CH$_2$)$_3$OH — 1.0
3: (CH$_2$)$_4$OH — 1.1
4: (CH$_2$)$_5$OH — 1.2
5: (CH$_2$)$_6$OH — 4.2
6: (CH$_2$)$_2$CH$_3$ — 3.9
7: (CH$_2$)$_3$CH$_3$ — 7.8
8: (CH$_2$)$_4$CH$_3$ — 6.2
9: (CH$_2$)$_5$CH$_3$ — 5.7
10: (CH$_2$)$_2$OMe — 1.7
11: (CH$_2$)$_3$OMe — 5.9
12: (CH$_2$)$_2$N(CH$_3$)$_2$ — 1.9
13: (CH$_2$)$_3$N(CH$_3$)$_2$ — 2.1
14: [ring] — 1.1
15: (CH$_2$)$_2$C$_6$H$_5$ — 17.9

This study

Figure S1

Structures of guaiazulene derivatives in our previous reports (B, C, D) and this study (E).
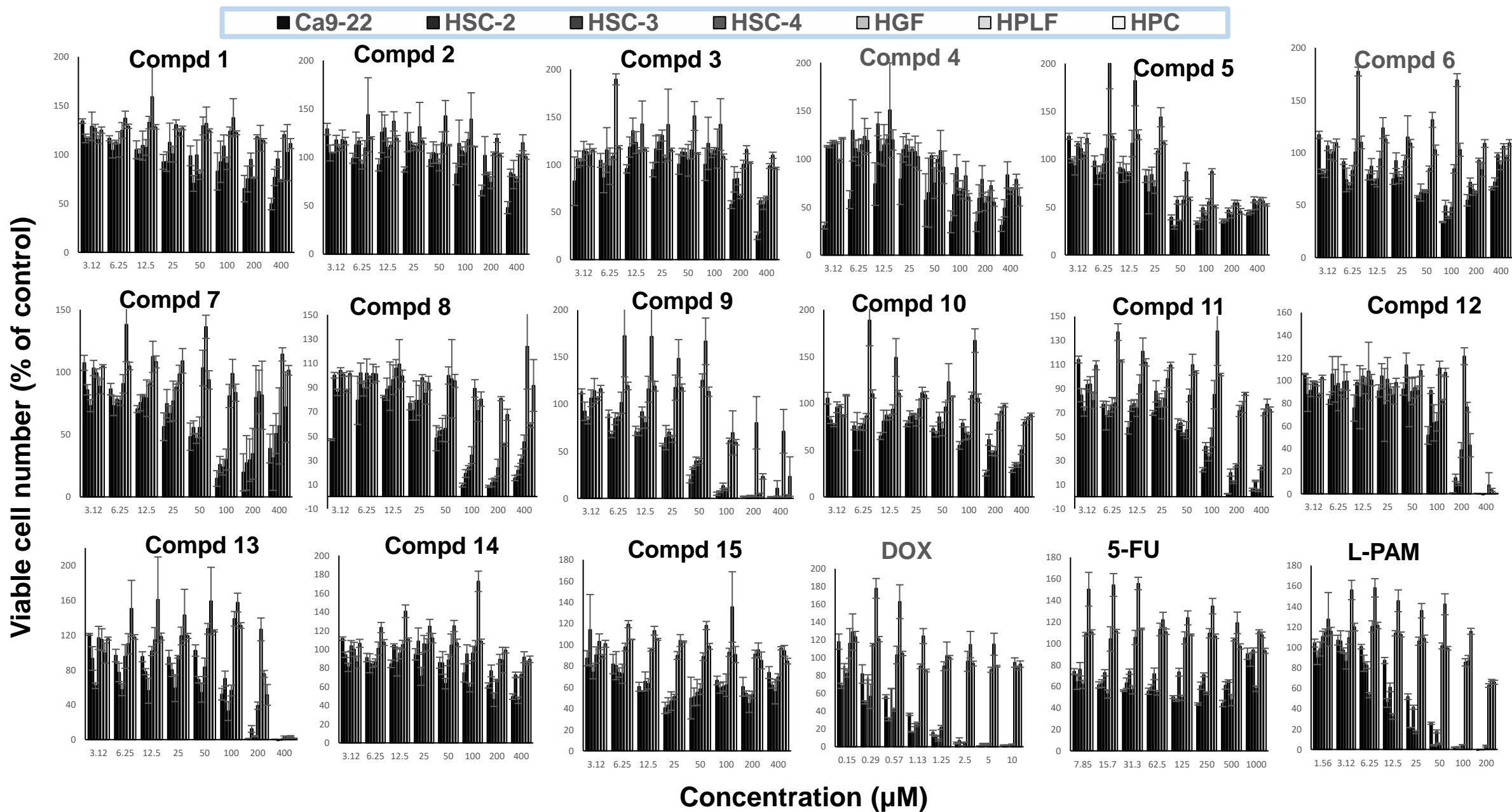
Figure S2 (1st experiment of dose-response of compounds 1-10, DOX, 5-FU and L-PAM
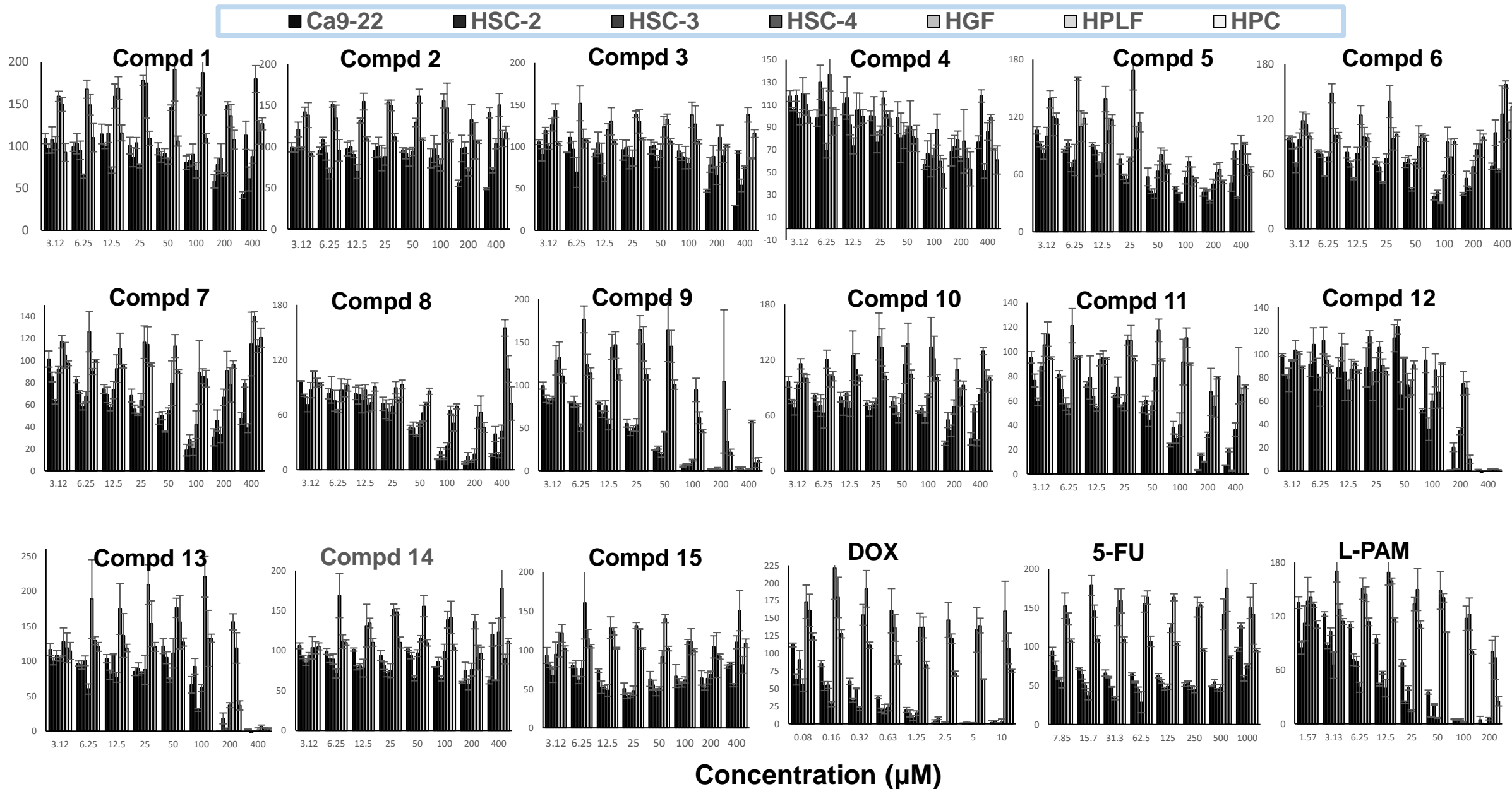
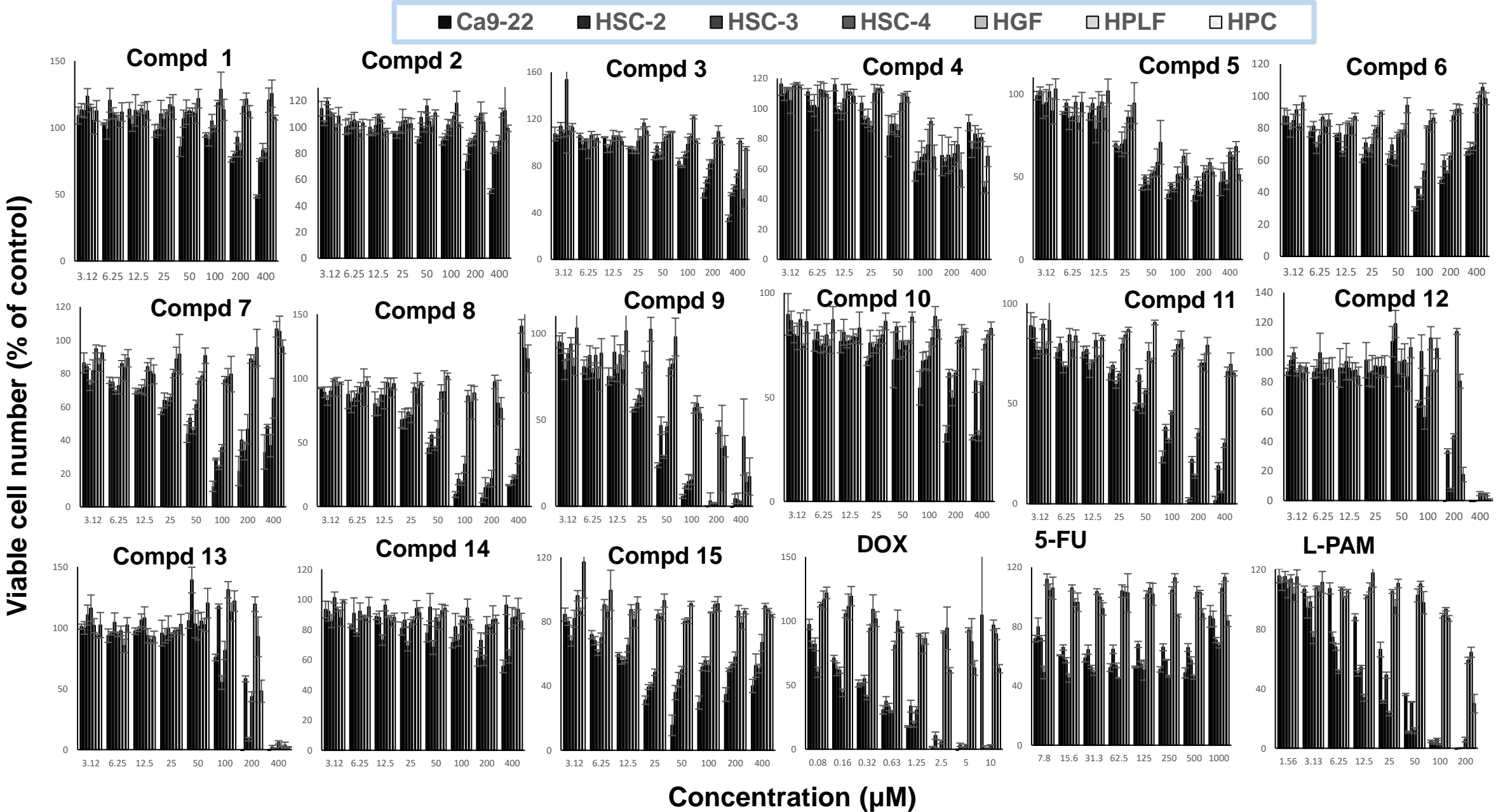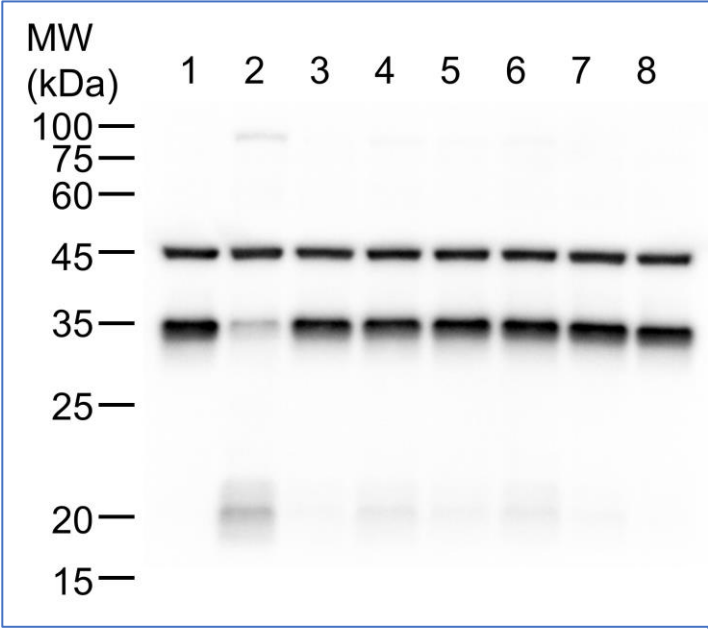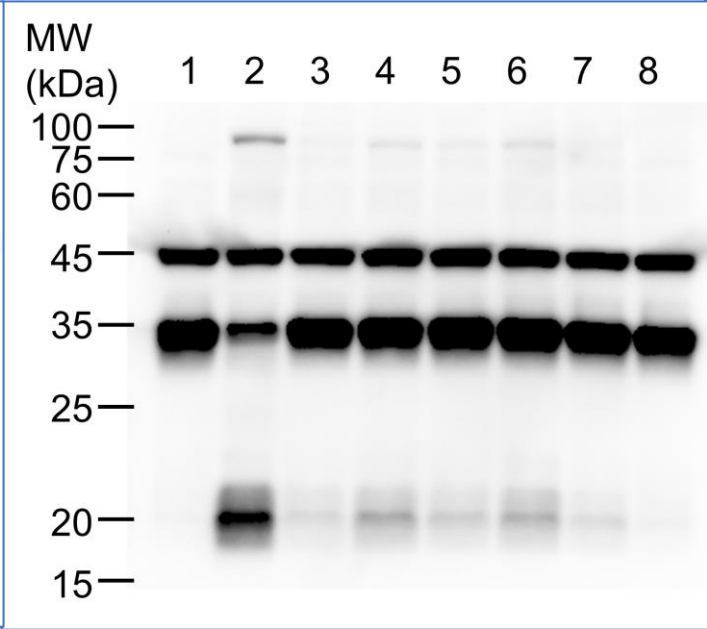**Figure S3** (2nd experiment of dose-response of compounds 1-10, DOX, 5-FU and L-PAM

Figure S4 (3rd experiment of dose-response of compounds 1-10, DOX, 5-FU and L-PAM
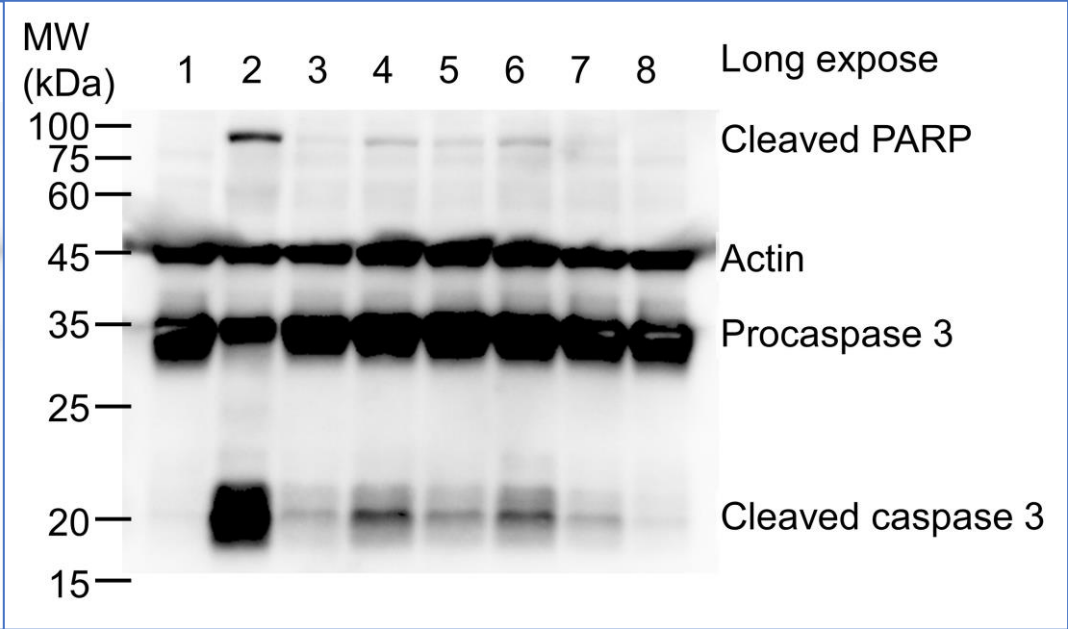
Sampling: 20210121   Applied protein: 15 µg

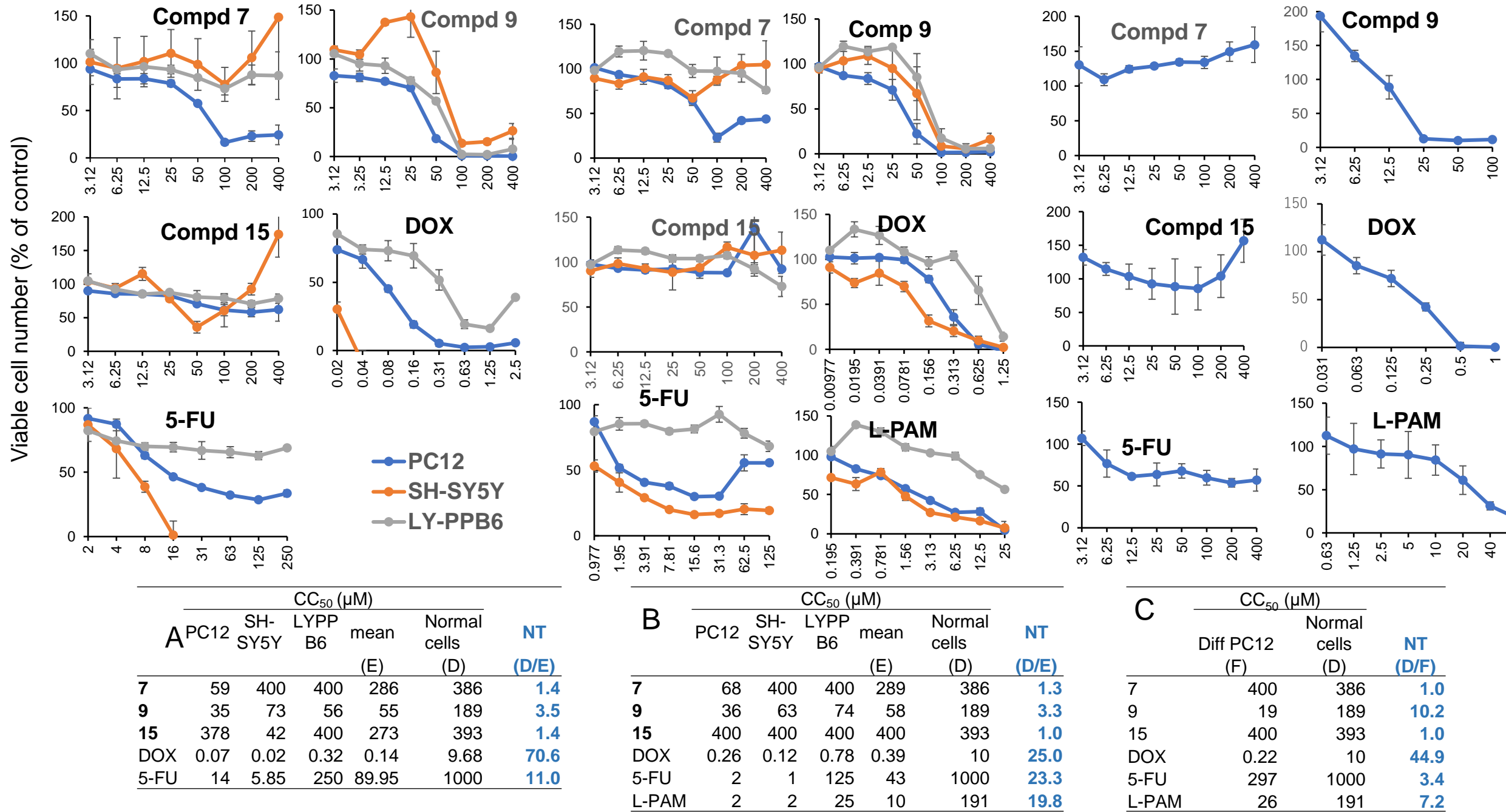**Figure S5.** Raw data of stained gel and images after short and long exposure (without and with contrast adjustment)

Figure S6 Neurotoxicity of compounds 7, 8 and 9 in comparison with reference compounds

A

	CC$_{50}$ (µM)					NT
	PC12	SH-SY5Y	LYPP B6	mean (E)	Normal cells (D)	(D/E)
7	59	400	400	286	386	1.4
9	35	73	56	55	189	3.5
15	378	42	400	273	393	1.4
DOX	0.07	0.02	0.32	0.14	9.68	70.6
5-FU	14	5.85	250	89.95	1000	11.0

B

	CC$_{50}$ (µM)					NT
	PC12	SH-SY5Y	LYPP B6	mean (E)	Normal cells (D)	(D/E)
7	68	400	400	289	386	1.3
9	36	63	74	58	189	3.3
15	400	400	400	400	393	1.0
DOX	0.26	0.12	0.78	0.39	10	25.0
5-FU	2	1	125	43	1000	23.3
L-PAM	2	2	25	10	191	19.8

C

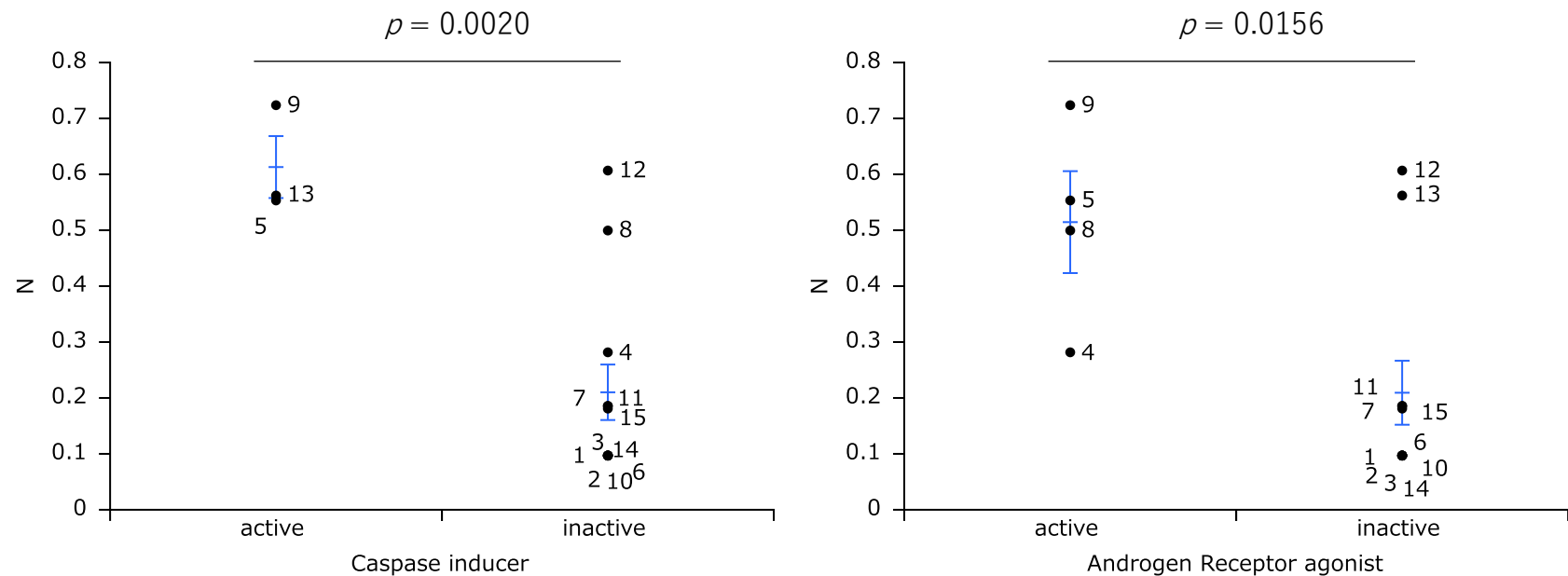|	CC$_{50}$ (µM)		NT
	Diff PC12 (F)	Normal cells (D)	(D/F)
7	400	386	1.0
9	19	189	10.2
15	400	393	1.0
DOX	0.22	10	44.9
5-FU	297	1000	3.4
L-PAM	26	191	7.2

Figure S7 Nuclear receptors and stress response pathways selectively associated with cytotoxicity against normal oral cells. The t-test was performed for cytotoxicity against humal normal oral cells (N) between azlene derivatives predicted as active and inactive in each biochemical pathway.
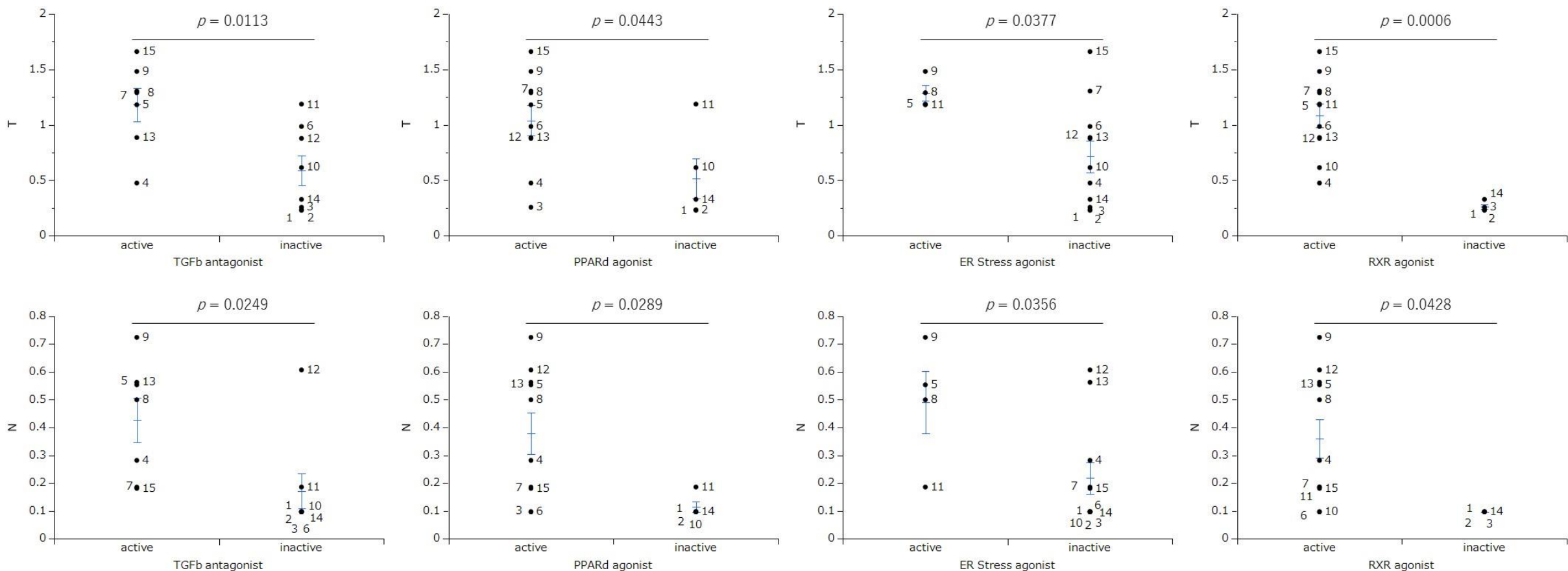
Figure S8 Nuclear receptors and stress response pathways non-selectively associated with cytotoxicity against both normal oral cells and oral squamous cell carcinoma cell lines. The *t*-test was performed for cytotoxicity against both normal and tumor cytotoxicity (N, T) between azulene derivatives predicted as active and inactive in each biochemical pathway.TGFb, PPARd, ER Stress, and RXR are transforming growth factor β, peroxisome proliferator activated receptor δ, endoplasmic reticulum stress, retinoid X receptor, respectively.

Exp. 1

	Ca9-22 (A)	HSC-2	HSC-3	HSC-4	mean (B)	SD	HGF (C)	HPLF	HPC	mean (D)	SD	TS (D/B)	TS (C/A)	PSE (100D/B²)	PSE (100C/A²)
1	327.7	400.0	400.0	400.0	381.9	36.2	400.0	400.0	400.0	400.0	0.0	1.0	1.2	0.3	0.4
2	363.7	333.3	400.0	400.0	374.3	32.2	400.0	400.0	400.0	400.0	0.0	1.1	1.1	0.3	0.3
3	247.3	400.0	400.0	333.3	345.2	72.4	400.0	400.0	400.0	400.0	0.0	1.2	1.6	0.3	0.7
4	64.4	141.4	400.0	326.7	233.1	156.5	400.0	400.0	400.0	400.0	0.0	1.7	6.2	0.7	9.6
5	43.9	32.4	111.5	39.9	56.9	36.7	400.0	400.0	115.1	305.0	164.5	5.4	9.1	9.4	20.8
6	66.4	87.9	77.3	90.7	80.6	11.1	400.0	400.0	400.0	400.0	0.0	5.0	6.0	6.2	9.1
7	36.3	59.6	46.0	59.0	50.2	11.2	400.0	270.7	400.0	356.9	74.7	7.1	11.0	14.2	30.4
8	49.2	55.7	56.7	62.2	55.9	5.3	400.0	172.3	400.0	324.1	131.4	5.8	8.1	10.4	16.5
9	29.7	34.4	41.7	39.1	36.2	5.3	400.0	126.1	126.3	217.5	158.1	6.0	13.5	16.6	45.3
10	117.3	283.7	183.7	186.0	192.7	68.5	400.0	400.0	400.0	400.0	0.0	2.1	3.4	1.1	2.9
11	63.0	79.6	55.3	92.0	72.5	16.5	400.0	400.0	400.0	400.0	0.0	5.5	6.3	7.6	10.1
12	105.3	154.0	118.7	151.0	132.3	24.0	326.0	272.3	190.7	263.0	68.1	2.0	3.1	1.5	2.9
13	105.2	134.0	34.6	133.3	101.8	46.8	322.3	270.0	215.3	269.2	53.5	2.6	3.1	2.6	2.9
14	373.3	333.3	195.0	400.0	325.4	91.2	400.0	400.0	400.0	400.0	0.0	1.2	1.1	0.4	0.3
15	19.1	19.8	55.3	24.3	29.6	17.3	400.0	400.0	333.3	377.8	38.5	12.8	20.9	43.0	109.6
DOX	0.41	0.16	0.43	0.20	0.30	0.14	10.00	7.08	10.00	9.03	1.68	30.0	24.4	9986.4	5929.5
5-FU	124.0	109.0	1000.0	72.6	326.4	449.6	1000.0	1000.0	1000.0	1000.0	0.0	3.1	8.1	0.9	6.5
L-PAM	27.1	11.9	19.3	9.3	16.9	8.0	200.0	200.0	200.0	200.0	0.0	11.8	7.4	70.2	27.3

CC50 (µM). Human oral squamous cell carcinoma cell lines: Ca9-22, HSC-2, HSC-3, HSC-4, mean, SD. Human normal oral cells: HGF, HPLF, HPC, mean, SD.

Exp. 2

	Ca9-22 (A)	HSC-2	HSC-3	HSC-4	mean (B)	SD	HGF (C)	HPLF	HPC	mean (D)	SD	TS (D/B)	TS (C/A)	PSE (100D/B²)	PSE (100C/A²)
1	287.3	400.0	392.3	400.0	369.9	55.2	400.0	400.0	400.0	400.0	0.0	1.1	1.4	0.3	0.5
2	376.7	400.0	400.0	400.0	394.2	11.7	400.0	400.0	400.0	400.0	0.0	1.0	1.1	0.3	0.3
3	194.0	400.0	400.0	400.0	348.5	103.0	400.0	400.0	400.0	400.0	0.0	1.1	2.1	0.3	1.1
4	400.0	400.0	283.0	400.0	370.8	58.5	400.0	400.0	400.0	400.0	0.0	1.1	1.0	0.3	0.3
5	72.8	37.7	33.7	221.7	91.5	88.6	400.0	291.7	200.0	297.2	100.1	3.2	5.5	3.6	7.5
6	80.3	86.3	28.4	400.0	148.7	169.5	400.0	400.0	400.0	400.0	0.0	2.7	5.0	1.8	6.2
7	47.2	49.5	26.6	57.7	45.2	13.2	400.0	400.0	400.0	400.0	0.0	8.8	8.5	19.5	18.0
8	46.3	43.1	36.4	49.1	43.7	5.5	264.7	228.2	184.0	225.6	40.4	5.2	5.7	11.8	12.3
9	28.7	22.8	25.0	22.7	24.8	2.8	331.3	174.7	96.5	200.8	119.6	8.1	11.5	32.6	40.1
10	140.7	327.3	157.3	400.0	256.3	127.6	400.0	400.0	400.0	400.0	0.0	1.6	2.8	0.6	2.0
11	57.1	72.4	38.3	73.7	60.4	16.6	400.0	266.7	400.0	355.6	77.0	5.9	7.0	9.8	12.3
12	103.7	159.7	74.5	137.0	118.7	37.4	267.3	261.0	151.7	226.7	65.0	1.9	2.6	1.6	2.5
13	123.0	156.7	76.5	145.7	125.5	35.5	342.0	316.0	186.3	281.4	83.4	2.2	2.8	1.8	2.3
14	400.0	400.0	333.3	400.0	383.3	33.3	400.0	400.0	400.0	400.0	0.0	1.0	1.0	0.3	0.3
15	24.0	14.0	15.5	16.6	17.5	4.4	400.0	400.0	400.0	400.0	0.0	22.8	16.7	130.2	69.6
DOX	0.5	0.2	0.3	0.1	0.2	0.2	10.0	10.0	10.0	10.0	0.0	40.7	22.1	16524.6	4901.9
5-FU	314.0	1000.0	20.4	9.5	336.0	464.6	1000.0	1000.0	1000.0	1000.0	0.0	3.0	3.2	0.9	1.0
L-PAM	38.7	11.0	17.5	4.9	18.0	14.7	200.0	200.0	155.0	185.0	26.0	10.3	5.2	56.9	13.3

CC50 (µM).

Exp.3

	Ca9-22 (A)	HSC-2	HSC-3	HSC-4	mean (B)	SD	HGF (C)	HPLF	HPC	mean (D)	SD	TS (D/B)	TS (C/A)	PSE (100D/B²)	PSE (100C/A²)
1	390	400	400	400	398	4.8	400	400	400	400	0.0	1.0	1.0	0.3	0.3
2	398	400	400	400	399	1.2	400	400	400	400	0.0	1.0	1.0	0.3	0.3
3	259	400	400	400	365	70.5	400	400	400	400	0.0	1.1	1.5	0.3	0.6
4	400	400	400	400	400	0.0	400	375	331	368	35.1	0.9	1.0	0.2	0.3
5	44	52	44	58	50	6.8	80	400	231	237	160.1	4.8	1.8	9.6	4.2
6	66	87	71	100	81	15.3	400	400	400	400	0.0	4.9	6.0	6.1	9.1
7	41	56	44	72	53	14.0	400	400	400	400	0.0	7.5	9.7	14.0	23.3
8	45	58	46	69	55	11.6	400	400	400	400	0.0	7.3	8.9	13.5	20.0
9	29	44	35	44	38	7.3	163	168	115	149	29.4	3.9	5.5	10.2	18.9
10	115	400	203	400	279	143.9	400	400	400	400	0.0	1.4	3.5	0.5	3.0
11	48	77	45	79	62	18.3	400	400	400	400	0.0	6.4	8.4	10.3	17.7
12	123	174	111	179	147	34.8	316	279	162	252	80.7	1.7	2.6	1.2	2.1
13	133	229	110	182	163	52.9	319	293	203	272	60.7	1.7	2.4	1.0	1.8
14	400	400	400	400	400	0.0	400	400	400	400	0.0	1.0	1.0	0.3	0.3
15	17	17	17	24	19	3.4	400	400	400	400	0.0	21.5	24.0	115.4	144.6
DOX	0.33	0.34	0.38	0.13	0.29	0.11	10	10	10	10	0.0	34.0	29.9	11536.5	8964.1
5-FU	136	1000	1000	17	538	535.5	1000	1000	1000	1000	0.0	1.9	7.4	0.3	5.4
L-PAM	38	13	23	7	20	13.8	200	200	165	188	20.0	9.3	5.2	45.9	13.7

CC50 (µM).

Mean of Exps 1, 2 and 3

	Ca9-22 (A)	HSC-2	HSC-3	HSC-4	mean (B)	HGF (C)	HPLF	HPC	mean (D)	TS (D/B)	TS (C/A)	PSE 100D/B²	PSE 100C/A²
1	335.1	400.0	397.4	400.0	383.1	400.0	400.0	400.0	400.0	1.0	1.2	0.3	0.4
2	379.3	377.8	400.0	400.0	389.3	400.0	400.0	400.0	400.0	1.0	1.1	0.3	0.3
3	233.4	400.0	400.0	377.8	352.8	400.0	400.0	400.0	400.0	1.1	1.7	0.3	0.7
4	288.1	313.8	361.0	375.6	334.6	400.0	391.6	376.9	389.5	1.2	1.4	0.3	0.5
5	53.5	40.8	63.2	106.5	66.0	293.3	363.9	181.9	279.7	4.2	5.5	6.4	10.2
6	71.1	86.9	59.0	196.9	103.5	400.0	400.0	400.0	400.0	3.9	5.6	3.7	7.9
7	41.6	55.1	38.9	62.9	49.6	400.0	356.9	400.0	385.6	7.8	9.6	15.7	23.1
8	46.7	52.4	46.3	60.1	51.4	354.9	266.8	328.0	316.6	6.2	7.6	12.0	16.2
9	29.3	33.9	33.8	35.2	33.0	298.2	156.1	112.5	189.0	5.7	10.2	17.3	34.8
10	124.2	337.0	181.3	328.7	242.8	400.0	400.0	400.0	400.0	1.7	3.2	0.7	2.6
11	55.9	76.5	46.3	81.6	65.1	400.0	355.6	400.0	385.2	5.9	7.2	9.1	12.8
12	110.7	162.7	101.3	155.6	132.6	303.2	270.7	168.0	247.3	1.9	2.7	1.4	2.5
13	120.5	173.1	73.6	153.6	130.2	327.7	293.0	201.6	274.1	2.1	2.7	1.6	2.3
14	391.1	377.8	309.4	400.0	369.6	400.0	400.0	400.0	400.0	1.1	1.0	0.3	0.3
15	19.9	16.8	29.4	21.5	21.9	400.0	400.0	377.8	392.6	17.9	20.1	81.7	101.0
DOX	0.4	0.2	0.4	0.1	0.3	10.0	9.0	10.0	9.7	34.5	25.1	12325.0	6270.0
5-FU	191.2	703.0	673.5	33.1	400.2	1000.0	1000.0	1000.0	1000.0	2.5	5.2	0.6	2.7
L-PAM	34.7	11.9	20.1	6.9	18.4	200.0	200.0	173.4	191.1	10.4	5.8	56.5	16.6

CC50 (µM).

Table S1 Cytotoxicity of 4,6,8-7trimethyl azulene amide derivatives and reference compounds against human oral squamous cell carcinoma cell lines and human normal oral cells, and TS and PSE values delineated from CC50 values. The data of 3 independent experiments and mean values are shown.

	r_pearson	r2	p_value		r_pearson	r2	p_value		r_pearson	r2	p_value		r_pearson	r2	p_value		r_pearson	r2	p_value
AATSC0v	0.8410942	0.70743946	8.5281E-05	vsurf_ID2	-0.70755708	0.50063702	0.00316975	AATSC0Z	-0.65236064	0.4255744	0.00839112	PEOE_VSA_P	-0.60192894	0.36231844	0.01758712	GATS1dv	-0.561438	0.31521263	0.02942116
GATS1se	-0.83325773	0.69431845	0.00011431	ATSC0c	-0.70674683	0.49949109	0.00322024	vsurf_D3	0.65139796	0.4243193	0.00852067	AATSC7i	0.60155067	0.3618632	0.01767718	MATS1s	0.56014385	0.31376113	0.02987893
FASA_H	0.81940379	0.67142257	0.00018535	ETA_dEpsilon	0.70670776	0.49943586	0.00322269	vsurf_D4	0.65124973	0.42412622	0.00854075	AATS0se	-0.60030223	0.36036277	0.01797694	nC	0.55964921	0.31320723	0.0300553
FASA_P	-0.81940369	0.6714224	0.00018535	SM1_Dzare	-0.70016623	0.49023275	0.00365452	vsurf_HB3	-0.65112747	0.42396699	0.00855735	Q_VSA_PPOS	-0.59806477	0.35768147	0.01852392	GATS7i	-0.55865593	0.31209645	0.03041185
GATS4s	0.81774718	0.66871046	0.00019585	AATSC0c	-0.70004773	0.49006682	0.00366275	AATSC0m	-0.64974086	0.42216318	0.00874734	AATSC0s	-0.59737757	0.35685996	0.01869445	EState_VSA2	-0.5565865	0.30978853	0.03116491
vsurf_CW5	-0.81702439	0.66752886	0.00020058	MAXaasC	0.69791244	0.48708177	0.00381353	Q_VSA_FPPC	-0.64915037	0.4213962	0.00882924	ATSC1s	0.59676898	0.35613322	0.01884648	MAXaaCH	0.55494481	0.30796374	0.03177224
AMID_C	0.81139109	0.6583555	0.00024077	vsurf_ID3	-0.6973885	0.48635072	0.00385127	vsurf_IW2	-0.64675264	0.41828898	0.009168	MATS7i	0.5949919	0.35401537	0.01929583	density	-0.5547097	0.30770286	0.03185993
ASA_P	-0.8057693	0.64926417	0.00028722	SM1_Dzpe	-0.6968113	0.48554598	0.00389319	chi1_C	0.64667355	0.41818667	0.00917934	Mse	-0.59409478	0.35294861	0.01952577	MID_C	0.55351938	0.30638371	0.03230674
vsurf_W5	-0.80175046	0.6428038	0.00032473	vsurf_ID5	-0.69039439	0.47664441	0.00438415	AATS1are	-0.64655277	0.41803049	0.00919669	MATS2se	0.59349774	0.35223957	0.01967995	MATS8se	-0.55332041	0.30616348	0.03238188
a_donacc	-0.7961373	0.6338346	0.00038373	SM1_Dzm	-0.68948565	0.47539046	0.00445747	GATS8i	-0.64627844	0.41767582	0.00923618	vsa_pol	-0.59239338	0.35092992	0.01996761	GATS8p	-0.55250144	0.30525784	0.03269256
vsurf_HL1	-0.79582979	0.63334505	0.0003872	SM1_DzZ	-0.68944675	0.47533682	0.00446063	GATS5s	0.64373621	0.41439631	0.00960851	AATSC1s	0.59128242	0.3496149	0.02026022	AATS0s	-0.55127157	0.30390034	0.03316331
AATS1i	-0.7952043	0.63234989	0.00039434	SM1_Dzse	-0.68835594	0.4738339	0.00454998	GATS5c	0.64323961	0.41375719	0.00968259	MATS8p	0.59097859	0.3492557	0.02034081	TASA	0.54946096	0.30190734	0.03386559
vsurf_CP	0.79291096	0.62870779	0.00042142	RASA	0.68811721	0.4735053	0.00456972	vsurf_D2	0.64120547	0.41114446	0.0099907	AATSC8p	0.59088547	0.34914564	0.02036556	Mare	-0.54898016	0.30137921	0.03405394
AATSC0p	0.78921951	0.62286744	0.0004682	opr_violation	0.68692287	0.47186303	0.00466951	vsurf_ID7	-0.6403085	0.40999497	0.01012897	Q_VSA_FPNE	-0.58954866	0.34756762	0.02072341	BIC1	-0.54699463	0.29920312	0.03484007
FNSA5	0.78537572	0.61681502	0.00052132	vsurf_W3	-0.68533991	0.46969079	0.00480443	GATS6c	0.63925736	0.40864997	0.0102929	RNCS	-0.58836052	0.3461681	0.02104548	EState_VSA9	-0.54311952	0.29497881	0.03641341
PEOE_VSA-1	0.78475391	0.6158387	0.00053036	vsurf_D5	0.68266608	0.46603297	0.00503932	GATS5are	0.63851263	0.40769838	0.01041029	PEOE_VSA_P	-0.58737815	0.34501309	0.02131464	PNSA5	0.53933043	0.29087732	0.0380026
vsurf_W4	-0.77246221	0.59669787	0.00073689	AATSC8i	0.68114863	0.46396345	0.00517661	vsurf_CW1	-0.63410102	0.4020841	0.01112725	ATSC7i	0.58732586	0.34495167	0.02132904	MINaaCH	0.53928134	0.29082437	0.03802352
vsurf_CW4	-0.76999267	0.59288871	0.00078536	TopoPSA	-0.68009975	0.46253567	0.00527322	SMR_VSA5	0.63404362	0.40201131	0.01113683	PEOE_VSA_F	-0.58634934	0.34380555	0.02159934	MATS2s	0.53881488	0.29032148	0.03822276
PEOE_VSA1	-0.76827196	0.59024181	0.00082064	TPSA	-0.68009973	0.46253564	0.00527323	vsurf_D6	0.63380662	0.40171084	0.01117643	PEOE_VSA_F	0.58634913	0.3438053	0.0215994	AATS5se	-0.5387478	0.2902492	0.03825147
AMID_h	-0.75769968	0.5741088	0.00106666	MATS8i	0.67832562	0.46012565	0.00543989	ATSC0are	-0.63294949	0.40062505	0.01132057	ATSC0s	-0.58547514	0.34278114	0.02184353	vsurf_ID8	-0.53831641	0.28978456	0.03843653
vsurf_HB5	-0.75683009	0.57279178	0.00108929	vsurf_ID4	-0.67827204	0.46005296	0.00544498	GATS5se	0.63113841	0.39833569	0.0116299	GCUT_SLOG	0.58398856	0.34104264	0.0222636	AMID_O	-0.53704929	0.28842194	0.03898396
GATS1are	-0.75540975	0.57064389	0.00112709	h_ema	-0.6777943	0.45940512	0.0054906	E_ang	-0.63038213	0.39738163	0.01176099	MATS8are	-0.58379561	0.34081776	0.02231846	vsurf_HB6	-0.53697036	0.28833717	0.03901826
MIC0	-0.74963639	0.56195471	0.00129181	AATS1se	-0.67716037	0.45854617	0.0055516	GATS5pe	0.62965638	0.39646716	0.01188788	vsurf_W6	-0.58313033	0.34004098	0.0225089	AATSC7p	0.53560953	0.28687757	0.03961294
FilterItLogS	-0.74938344	0.56157555	0.00129945	vsurf_ID1	-0.67656951	0.45774631	0.00560893	SIC0	-0.62935612	0.39608912	0.01194068	MATS2are	0.58311628	0.3400246	0.02251293	vsurf_R	0.53486134	0.28607665	0.03994285
PEOE_VSA6	0.74444567	0.55419936	0.00145601	ETA_epsilon_	-0.6749637	0.455576	0.00576711	GATS1s	-0.62911365	0.39578399	0.01198345	ATSC8p	0.58297663	0.33986176	0.02255305	h_emd	-0.53434526	0.28552485	0.04017156
vsurf_HB4	-0.73927012	0.5465203	0.00163608	SM1_Dzp	0.67308754	0.45304684	0.00595637	vsurf_CW6	-0.62796234	0.39433671	0.01218818	GATS6pe	0.58134333	0.33796007	0.02302627	AATS0pe	-0.53389923	0.28504839	0.04037002
SLogP	0.7390612	0.54621146	0.00164371	BIC0	-0.67171144	0.45119626	0.00609827	SMR_VSA1	-0.62662334	0.3926568	0.0124297	vsurf_HB1	-0.57808402	0.33418114	0.02399318	ATSC7p	0.53356993	0.28469687	0.040517
SlogP	0.73905793	0.54620662	0.00164383	MID_h	-0.67144934	0.45084422	0.0061256	AATSC0se	-0.62564902	0.39143669	0.01260775	PEOE_VSA_F	-0.57582497	0.33157439	0.02468126	MINaasC	0.53294726	0.28403279	0.04079602
ETA_dAlpha_B	-0.73451808	0.53951681	0.0018168	GATS3c	0.6707835	0.44995051	0.00619545	vsurf_IW4	-0.62425279	0.38969155	0.01286635	ZMIC1	0.57431272	0.32983511	0.02515017	AATS7p	0.53253159	0.28358989	0.04098307
logP(o/w)	0.72697365	0.52849069	0.0021364	vsurf_IW5	-0.67064467	0.44976428	0.0062101	ETA_dEpsilon	-0.62128127	0.38599042	0.01343041	vsurf_D7	0.57416598	0.32966657	0.02519603	MATS7p	0.53242441	0.28347575	0.04103141
h_logS	-0.72563495	0.52654609	0.00219754	ASA_H	0.67011081	0.44904849	0.00626667	ATSC0se	-0.61729156	0.38104887	0.01421765	GATS6s	0.57398556	0.32945942	0.0252525	vsurf_W2	-0.529017	0.27985899	0.04259025
ETA_dPsi_A	-0.72530593	0.52606869	0.00221278	Q_VSA_POL	-0.66946078	0.44817773	0.00633609	vsurf_ID6	-0.61542145	0.37874356	0.01459871	vsurf_D8	0.57066625	0.32565996	0.02630867	nO	-0.52852751	0.27934133	0.04281774
vsurf_A	-0.72465225	0.52512088	0.00224332	h_logD	0.66593371	0.4434677	0.00672343	DPSA5	-0.6145084	0.37762058	0.0147876	AATS0are	-0.57049223	0.32546138	0.02636495	MATS7v	0.52580347	0.27646928	0.04410025
Q_VSA_FHYD	0.72191997	0.52116845	0.00237461	Q_VSA_HYD	0.6655985	0.44302136	0.00676119	GATS4c	0.61417038	0.37720526	0.01485801	chi0_C	0.56919809	0.32398647	0.02678635	vsurf_Wp5	-0.52337631	0.27392276	0.04526676
Q_VSA_FPOL	-0.72191996	0.52116843	0.00237461	vsurf_HB2	-0.66355564	0.44030609	0.00699494	AATS1pe	-0.61379031	0.37673855	0.01493748	IC1	-0.56832963	0.32299857	0.02707199	MINdssC	0.52106428	0.27150799	0.04639901
vsurf_CW3	-0.71857731	0.51635335	0.00254354	GATS4se	0.66173079	0.43788764	0.00720907	ATSC0pe	-0.61363801	0.37655161	0.01496942	SsOH	-0.5681269	0.32276818	0.027139	GATS2s	-0.52065734	0.27108406	0.04660044
lip_acc	-0.71843266	0.51614549	0.00255106	GATS4pe	0.65843307	0.43353411	0.00760909	ATSC1c	0.6135284	0.3764171	0.01499244	PEOE_VSA+4	-0.56785491	0.3224592	0.0272291	GATS7v	-0.51948808	0.26986786	0.04718281
ETA_epsilon_2	-0.7176485	0.51501937	0.00259215	ATSC8i	0.65780004	0.43270089	0.00768783	vsurf_HL2	-0.60837424	0.37011922	0.01610606	PEOE_VSA_P	-0.56785491	0.3224592	0.0272291	DCASA	-0.51931874	0.26969196	0.0472676
logS	-0.71503937	0.51128129	0.00273268	AATSC0are	-0.65640788	0.43087131	0.00786325	GATS6are	0.60807504	0.36975525	0.01617261	nHBDon	-0.56785491	0.3224592	0.0272291	vsurf_CW2	-0.51911546	0.26948086	0.04736953
SM1_Dzv	0.71335858	0.50888047	0.00282639	MIC1	-0.65622248	0.43062795	0.00788685	AATSC1c	0.60662344	0.367992	0.01649849	MATS8pe	-0.56494367	0.31916135	0.02820771	PM3_HF	0.51860268	0.26894874	0.04762736
h_logP	0.71042416	0.50470249	0.00299613	GATS4are	0.65614381	0.4305247	0.00789688	GATS6se	0.60550791	0.36663982	0.01675234	VSA_EState3	-0.5641704	0.31828624	0.02847206	AATSC7v	0.51841163	0.26875062	0.04772369
a_ICM	-0.7086862	0.50223613	0.00310044	AATSC0pe	-0.65558933	0.42979736	0.00796785	EState_VSA8	0.60496148	0.36597839	0.01687778	MATS2pe	0.56352279	0.31755793	0.02869489	ATSC7v	0.51743375	0.26773769	0.04821699
IC0	-0.70868603	0.50223589	0.00310045	vsurf_D1	0.65423755	0.42802677	0.00814297	MINssCH2	0.603711	0.36446697	0.01716756	chi1v_C	0.5632337	0.31723221	0.02879478	vsurf_Wp3	-0.51706302	0.26735416	0.04840776
SM1_Dzi	-0.70834328	0.50175021	0.00312136	vsurf_IW3	-0.65264669	0.4259477	0.00835292	PEOE_VSA-6	-0.60192894	0.36231845	0.01758712					GATS1pe	-0.51548378	0.26572352	0.04921796

Table S2 220 chemical descriptors that significantly (p<0.05) correlate to selective toxicity against OSCC cells